Remarks

Claims 1, 2, 4, 5, 6, and 8 are amended; claims 7,9 and 10 are cancelled; and new claims 15 and 16 are presented by foregoing Amendment. Entry of the Amendment and favorable consideration thereof is respectfully requested.

Claim Rejections – 35 U.S.C. §112

Claims 5 and 6 have been rejected under 35 USC §112 as lacking enablement in the specification. By the foregoing amendment, claims 5 and 6 are amended to restrict them to the subject matter indicated by the Examiner to be enabled by the specification.

Claim Rejections – 35 U.S.C. §112

Claim 4 has been rejected under 35 USC §112 as indefinite and lacking antecedent basis. By the foregoing amendment, claims 4 is amended to address the Examiner's rejections.

Claim Rejections – 35 U.S.C. §102

Anticipation By Guo

The Examiner has rejected claims 1 and 3 under 35 USC §102(b) as anticipated by Guo, Drug Delivery, 7:113-116 (2000). Guo discloses making flexible lethicin vesicles containing insulin. Guo is clearly directed at making liposome structures, particularly, flexible "vesicles" in which sodium cholate is added to the vesicle structures.

In contrast, the claims of the present application are for a method of formulating an insulin composition using a non-liposome crystal non-polar phosphatidylcholine carrier. This method of formulating an insulin composition using non-liposome multilamellar crystal non-polar phosphatidylcholine is not anticipated by Guo's processes of mak-

ing flexible vesicles by incorporating sodium cholate. Accordingly, the presently claimed invention is not anticipated by Guo et al.

Anticipation By Modi

The Examiner has rejected claims 1 and 3 under 35 USC §102(b) as anticipated by Modi (US 6,214,375). Modi discloses making a mixed liposome pharmaceutical formulation with multilamellar vesicles, comprising a proteinic pharmaceutical agent, water, an alkali metal lauryl sulphate in a concentration of from 1 to 10 wt./wt. % of the total formulation, at least one membrane-mimetic amphiphile and at least one phospholipid. Modi is clearly directed at making liposome structures, as they are described by Modi's disclosure as "mixed multi-lamellar vesicles". (Col. 6, line 42).

In contrast, the claims of the present application are for a method of formulating an insulin composition using a non-liposome crystal non-polar phosphatidylcholine carrier. This method of formulating an insulin composition using non-liposome multilamellar crystal non-polar phosphatidylcholine is not anticipated by Modi's processes of making mixed liposome pharmaceutical formulation with multilamellar vesicles.

Anticipation By Hansen

The Examiner has rejected claim 1 under 35 USC §102(b) as anticipated by Hansen (US 4,614,730). Hansen discloses making a solution of insulin and water and stabilizing it with a phosphatidylcholine to stabilize the solution. The solution is adapted for parental administration.

The claims of the present application specify "mixing an insulin solution into said [phosphatidylcholine] carrier to entrap said insulin within said [phosphatidylcholine] carrier"; in other words the invention contemplates a carrier made up of a sufficient amount of non-liposome crystal non-polar phosphatidylcholine that will it will be capable of trapping the insulin in the crystal structure.

In contrast, Hansen uses a very small quantity of phosphatidylcholine in order to generate a monomolecular lipid layer at the air/insulin solution interface of a container (See Col. 3, line 45-Col. 4, line 3). The quantity of phosphatidylcholine described used by Hansen in the insulin solution is insufficient to "entrap said insulin within said [phosphatidylcholine] carrier."

.

The presently claimed method of formulating an insulin composition is not anticipated by Hansen's processes of stabilizing an insulin/water solution by addition of a small quantity of phosphatidylcholine.

Claim Rejections – 35 USC § 103

The Examiner has rejected claims 1-14 under 35 USC §103 as unpatentable over Kikuchi (US Patent 4,687,661) in view of Patel (US Patent 6,294,192), Chaiyawat (US Patent 6,538,061), Brieva (US Patent 5,985,298), and Modi (US 6,214,375).

Kikuchi (US Patent 4,687,661) discloses preparation of liposomes by mixing membrane components such as phospholipids with an organic water soluble solvent and dispersing it into an aqueous medium.

Patel et al. (US 6,294,192) is directed at the formulation of hydrophobic therapeutic compounds with a hydrophilic surfactant and a hydrophobic surfactant to solubilize the hydrophobic therapeutic compounds; including use of polyethylene glycol ("PEG") compounds. Patel does not mention the combination of such PEGs with phosphatidylcholines to produce the structures described within the instant invention.

Brieva (US 5,985,298) is directed at a trimethylated silica/ polysiloxane polymer mascara compositions.

Chaiyawat (US 6,538,061) is directed polyether siloxane compositions for cosmetic compositions.

The claims of the present application are for a method of formulating an insulin composition using a non-liposome crystal non-polar phosphatidylcholine carrier. This method of formulating an insulin composition using non-liposome multilamellar crystal non-polar phosphatidylcholine is not disclosed or suggested by the references.

Specifically, the disclosure of Kikuchi teaches away from the loosely arranged phosphatidylcholine component entrapping a macromolecular drug as claimed in the present invention, and instead suggests methods of making liposomes. Kikuchi's liposomes are prepared from lipids and a solvent. Kikuchi's liposomes are spherical vesicles formed by hydrating a phospholipid. They contain a water-filled central core with a water-soluble substances or active agent incorporated in the core. Liposomes flexible and deformable to pass through pores

The claims of the present application are directed at a method of formulating topical insulin in a non-liposome non-polar crystal phosphatidylcholine. Crystalline forms are by definition relatively nonflexible or inflexible. The method of the invention results in a crystal phosphatidylcholine carrier entrapping insulin. The phosphatidylcholine forms a disordered, multilamellar structure entrapping the macromolecule.

In summary, Kikuchi discloses a method of making a different physical structure - a polar liposome structure – which is not the same as the non-polar, loose crystal structure claimed in the present application. The disclosure of Kikuchi teaches away from the method of forming a loosely arranged phosphatidylcholine composition entrapping a macromolecular drug of the present invention. While Kikuchi lists phosphatidylcholine among a long list of possible lipids (See Col. 2, lines 22-28), it does not disclose or teach a method of formulating it with insulin in a crystal form to entrap a molecule and stabilize it at room temperature. The temperature stabilizing effects of phosphatidylcholine by itself would not have been obvious to one of ordinary skill in the art.

The present invention provides a method of formulating topical insulin using a carrier that is stable at room temperatures and provides the advantage of longer shelf-life and

the ability to store and carry macromolecular drugs without needing refrigeration, in addition to ease of administration through transdermal delivery. The present invention does not use the techniques described in Kikuchi or the cited prior art, and is neither disclosed by nor obvious in view of the disclosure of Kikuchi nor by the combination of references. It is submitted that the presently claimed invention is patentable over Kikuchi in view of Patel, Chaiyawat, Brieva, and Modi, and issuance of a Notice of Allowance is respectfully requested.

Respectfully submitted,

June 20, 2007

Stephen P. McNamara, Registration No. 32,745
Attorney for Applicants
ST.ONGE STEWARD JOHNSTON & REENS LLC
986 Bedford Street
Stamford, CT 06905-5619
Tel. 203 324-6155